Influence of Catalyst Structure and Reaction Conditions on anti- versus syn-Aminopalladation Pathways in Pd-Catalyzed Alkene Carboamination Reactions of N-Allylsulfamides

Ryan M. Fornwald,[a] Jonathan A. Fritz,[b] and John P. Wolfe*[a]

chem_201402258_sm_miscellaneous_information.pdf
General Considerations

Preparation and Characterization of N-Allysulfamide Substrate Precursors

Preparation and Characterization of Sulfamide Substrates

Assignment of Stereochemistry

References

Copies of NMR Spectra

**General:** All reactions were carried out under a nitrogen atmosphere in flame-dried glassware unless otherwise noted. All reagents were obtained from commercial sources and were used as obtained unless otherwise noted. N-Benzyl-2-oxooxazolidine-3-sulfonamide,¹ N-(4-methoxyphenyl)-2-oxooxazolidine-3-sulfonamide,¹ N-benzylcyclopent-2-enylamine,² N-benzylbut-3-en-2-ylamine,³ N-benzylallylamine,⁴ N-benzylmethallylamine,⁵ 1-allyl-1,3-bis-benzylsulfamide (1a),¹ 1-allyl-1-benzyl-3-(4-methoxyphenyl)sulfamide (1f),¹ 1,3-bis-benzyl-1-cyclopent-2-enylsulfamide (12),¹ (Z)-1-(3-d-allyl)-1-methyl-3-(4-nitrophenyl)urea (20),⁶ 1-benzyl-
5-chloro-1H-indole,\textsuperscript{7} 4-cyanophenyl triflate,\textsuperscript{8} 4-chlorophenyl triflate,\textsuperscript{8} 4-methoxyphenyl triflate,\textsuperscript{8} 3-trifluoromethylphenyl triflate,\textsuperscript{9} 2-methylphenyl triflate,\textsuperscript{10} and 3,4-methylenedioxyphenyl triflate\textsuperscript{11} were prepared according to published procedures. Bulk quantities of lithium tert-butoxide and sodium tert-butoxide were stored in a glove box and removed in small amounts (ca. 1–2 g) that were consumed within a few days. Toluene, THF, diethyl ether and dichloromethane were purified using a GlassContour solvent purification system.

**Preparation and Characterization of N-allylsulfamide Substrate Precursors**

\textbf{N-\textit{(4-Methoxybenzyl)}-2-oxooxazolidine-3-sulfonamide (S1a).} The title compound was prepared from chlorosulfonyl isocyanate (0.87 mL, 10 mmol), 2-chloroethanol (0.67 mL, 10 mmol), and \textit{p}-methoxybenzylamine (1.5 mL, 11 mmol), according to a procedure analogous to that described by Stahl.\textsuperscript{1} This procedure afforded 1.56 g (54\%) of the title compound as a white solid: mp = 115–117 °C. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.24 (d, \(J = 9.0\) Hz, 2 H), 6.88 (d, \(J = 8.6\) Hz, 2 H), 5.64 (t, \(J = 6.2\) Hz, 1 H), 4.25–4.19 (m, 4 H), 3.83 (dd, \(J = 7.1, 8.7\) Hz, 2 H), 3.79 (s, 3 H); \textsuperscript{13}C NMR (126 MHz, CDCl\textsubscript{3}) \(\delta\) 159.7, 153.2, 129.6, 127.3, 114.2, 62.5, 55.4, 47.6, 44.8; IR (film) 3291, 1748, 1360, 1149 cm\textsuperscript{-1}. MS (ESI) 309.0511 (309.0516 calcd for C\textsubscript{11}H\textsubscript{14}N\textsubscript{2}O\textsubscript{5}S, M + Na\textsuperscript{+}).

\textbf{N-Methyl-2-oxooxazolidine-3-sulfonamide (S1b).} The title compound was prepared from chlorosulfonyl isocyanate (3.5 mL, 40 mmol), 2-chloroethanol (2.7 mL, 40 mmol) and methylamine (7.5 mL, 60 mmol, 8 M solution in ethanol), according to a procedure analogous to that described by Stahl except the workup was modified such that triethylamine hydrochloride was removed by column chromatography.\textsuperscript{1} This procedure afforded 5.24 g (73\%) of the title compound as a white solid: mp = 103–105 °C. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 5.38 (s, 1 H), 4.48 (dd, \(J = 7.1, 8.6\) Hz, 2 H), 4.09 (dd, \(J = 7.1, 8.6\) Hz, 2 H), 2.83 (d, \(J = 5.2\) Hz, 3 H); \textsuperscript{13}C NMR
(126 MHz, CDCl$_3$) $\delta$ 153.5, 62.6, 45.2, 30.0; IR (film) 3238, 1750, 1354, 1153 cm$^{-1}$. MS (ESI) 203.0098 (203.0097 calcld for C$_4$H$_8$N$_2$O$_4$S, M + Na$^+$).

$N$-(tert-Butyl)-2-oxooxazolidine-3-sulfonamide (S1c). The title compound was prepared from chlorosulfonyl isocyanate (3.5 mL, 40 mmol), 2-chloroethanol (2.7 mL, 40 mmol), and tert-butylamine (4.6 mL, 44 mmol) according to a procedure analogous to that described by Stahl. This procedure afforded 7.21 g (81%) of the title compound as a white solid: mp = 139–140 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.30 (s, 1 H), 4.40 (dd, $J = 7.1$, 8.7 Hz, 2 H), 4.04 (dd, $J = 7.1$, 8.7 Hz, 2 H), 1.35 (s, 9 H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 153.4, 62.4, 55.7, 44.5, 29.4; IR (film) 3250, 1756, 1362, 1145 cm$^{-1}$. MS (ESI) 245.0574 (245.0566 calcld for C$_7$H$_{14}$N$_2$O$_4$S, M + Na$^+$).

$N$-Allyl-2-oxooxazolidine-3-sulfonamide (S1d). The title compound was prepared from chlorosulfonyl isocyanate (5.2 mL, 60 mmol), 2-chloroethanol (4.0 mL, 60 mmol), and allylamine (5.0 mL, 66 mmol) according to a procedure analogous to that described by Stahl except the workup was modified such that triethylamine hydrochloride was removed by column chromatography. This procedure afforded 7.5 g (61%) of the title compound as a white solid: mp = 83–85 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.88 (ddt, $J = 6.0$, 10.2, 17.0 Hz, 1 H), 5.57–5.46 (m, H), 5.40–5.23 (m, 2 H), 4.45 (dd, $J = 6.6$, 9.1 Hz, 2 H), 4.07 (dd, $J = 6.6$, 9.3 Hz, 2 H), 3.78 (tt, $J = 1.4$, 6.2 Hz, 2 H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 153.4, 132.4, 118.6, 62.6, 46.5, 45.2; IR (film) 3286, 1747, 1356, 1146 cm$^{-1}$. MS (ESI) 229.0257 (229.0253 calcld for C$_6$H$_{10}$N$_2$O$_4$S, M + Na$^+$).
General Procedure A: Synthesis of N-Allyl Sulfamides

A flame dried flask was charged with the appropriate oxazolidinone substrate S1 (1.0 equiv), 4-dimethylaminopyridine (0.2 equiv), and a stir bar, then was evacuated and backfilled with N₂. Acetonitrile was added, followed by Et₃N (3.0 equiv), and then the reaction vessel was placed in an oil bath at 80 °C and stirred for 30 minutes. The appropriate amine (1.1 equiv) was added and the resulting mixture was heated to reflux overnight (approximately 16 hours). The mixture was cooled to rt, solvent was removed via rotary evaporation, and the residue was partitioned between CH₂Cl₂ and 1 M HCl. The aqueous layer was extracted with CH₂Cl₂, the combined organic layers were washed with brine and dried over anhydrous Na₂SO₄. Solvent was removed in vacuo and the resulting residue was purified by flash chromatography on silica gel.

1-Allyl-3-benzyl-1-methylsulfamide (1b). The title compound was prepared from N-benzyl-2-oxooxazolidine-3-sulfonamide (1.9 g, 7.42 mmol) and N-allylmethylamine (0.78 mL, 8.16 mmol) according to general procedure A except the reaction temperature was lowered to 60 °C prior to addition of the amine. This procedure afforded 1.41 g (79%) of the title compound as a white solid: mp = 32–34 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.39–7.25 (m, 5 H), 5.77 (ddt, J = 6.3, 10.1, 16.6 Hz, 1 H), 5.30–5.15 (m, 2 H), 4.45–4.31 (m, 1 H), 4.19 (d, J = 6.0 Hz, 2 H), 3.71 (d, J = 6.4 Hz, 2 H), 2.73 (s, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 137.0, 132.9, 128.7, 128.0, 127.9, 118.8, 53.2, 47.4, 34.3; IR (film) 3294, 1325, 1144 cm⁻¹. MS (ESI) 241.1010 (241.1005 calcd for C₁₁H₁₆N₂O₂S, M + H⁺).

1-Allyl-3-benzyl-1-methylsulfamide (1c). The title compound was prepared from S1a (1.2 g, 4.2 mmol) and N-allylbenzylamine (0.72 mL, 8.16 mmol) according to general...
procedure A. This procedure afforded 1.18 g (81%) of the title compound as a white solid: mp = 64–66 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40–7.25 (m, 5 H), 7.18 (d, $J$ = 8.5 Hz, 2 H), 6.85 (d, $J$ = 8.1 Hz, 2 H), 5.83 (ddt, $J$ = 6.5, 10.2, 16.8 Hz, 1 H), 5.25–5.13 (m, 2 H), 4.38 (s, 2 H), 4.17 (t, $J$ = 6.0 Hz, 1 H), 4.10 (d, $J$ = 5.9 Hz, 2 H), 3.79 (s, 3 H), 3.75 (d, $J$ = 6.6 Hz, 2 H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 159.3, 136.3, 132.8, 129.4, 128.7, 128.6, 128.6, 127.8, 119.5, 114.1, 55.3, 50.5, 49.9, 46.8; IR (film) 3286, 1243, 1145 cm$^{-1}$. MS (ESI) 369.1239 (369.1243 calcd for C$_{18}$H$_{22}$N$_2$O$_3$S, M + Na$^+$).

1-Allyl-1-benzyl-3-methylsulfamide (1d). The title compound was prepared from S1b (2.60 g, 14.4 mmol) and N-allylbenzylamine (2.49 mL, 15.9 mmol) according to general procedure A. This procedure afforded 2.91 g (84%) of the title compound as a clear, colorless oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40–7.25 (m, 5 H), 5.84 (ddt, $J$ = 6.6, 10.2, 16.8 Hz, 1 H), 5.27–5.12 (m, 2 H), 4.36 (s, 2 H), 4.01 (s, 1 H), 3.72 (d, $J$ = 6.7 Hz, 2 H), 2.67 (d, $J$ = 5.3 Hz, 3 H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 136.3, 132.7, 128.6, 128.5, 127.8, 119.5, 50.4, 49.7, 29.2; IR (film) 3311, 1312, 1144 cm$^{-1}$. MS (ESI) 263.0828 (263.0825 calcd for C$_{11}$H$_{16}$N$_2$O$_2$S, M + Na$^+$).

1-Allyl-1-benzyl-3-tert-butylsulfamide (1e). The title compound was prepared from S1c (2.22 g, 10 mmol) and N-allylbenzylamine (1.72 mL, 11 mmol) according to general procedure A. This procedure afforded 2.17 g (77%) of the title compound as a white solid: mp = 48–49 °C. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.35–7.24 (m, 5 H), 5.86 (ddt, $J$ = 6.6, 10.1, 16.9 Hz, 1 H), 5.26–5.07 (m, 2 H), 4.35 (s, 2 H), 3.83 (s, 1 H), 3.71 (d, $J$ = 6.8 Hz, 2 H), 1.33 (s, 9 H); $^{13}$C NMR (126 MHz, CDCl$_3$) $\delta$ 136.3, 132.9, 128.8, 128.5, 127.7, 119.3, 54.5, 50.4, 49.6, 30.0; IR (film) 3275, 1322, 1131 cm$^{-1}$. MS (ESI) 305.1295 (305.1294 calcd for C$_{14}$H$_{22}$N$_2$O$_2$S, M + Na$^+$).
1-Allyl-3-benzyl-1-tert-butylsulfamide (1g). The title compound was prepared from N-benzyl-2-oxooxazolidine-3-sulfonamide (2.56 g, 10 mmol) and N-allyl-tert-butylamine (1.64 mL, 11 mmol) according to general procedure A. This procedure afforded 2.06 g (73%) of the title compound as a white solid: mp = 75–76 °C. \( ^1H \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 7.41–7.28 (m, 5 H), 5.99 (ddt, \( J = 5.9, 10.2, 17.2 \) Hz, 1 H), 5.29–5.12 (m, 2 H), 4.24 (t, \( J = 6.4 \) Hz, 1 H), 4.17 (d, \( J = 6.1 \) Hz, 2 H), 3.97 (dt, \( J = 1.5, 6.0 \) Hz, 2 H), 1.48 (s, 9 H); \( ^13C \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 137.3, 136.8, 128.7, 128.1, 127.9, 116.5, 59.2, 49.3, 47.3, 29.7; IR (film) 3327, 1317, 1135 cm\(^{-1}\). MS (ESI) 305.1295 (305.1294 calcd for C\(_{14}\)H\(_{22}\)N\(_2\)O\(_2\)S, M + Na\(^+\)).

1,3-Bis-allylsulfamide (1h). The title compound was prepared from S1d (2.06 g, 10 mmol) and allylamine (1.5 mL, 20 mmol) according to general procedure A except the reaction temperature was lowered to 53 °C prior to addition of the amine. This procedure afforded 1.30 g (74%) of the title compound as a white solid: mp = 77–78 °C. \( ^1H \) NMR (500 MHz, CDCl\(_3\)) \( \delta \) 5.90 (dddd, \( J = 5.6, 6.3, 10.4, 17.0 \) Hz, 2 H), 5.38–5.16 (m, 4 H), 4.31–4.13 (m, 2 H), 3.70 (tt, \( J = 1.5, 6.1 \) Hz, 4 H); \( ^13C \) NMR (126 MHz, CDCl\(_3\)) \( \delta \) 133.4, 117.7, 45.7; IR (film) 3277, 1312, 1146 cm\(^{-1}\). MS (ESI) 177.0692 (177.0692 calcd for C\(_6\)H\(_{12}\)N\(_2\)O\(_2\)S, M + H\(^+\)).

1,3-Bis-benzyl-1-but-3-en-2-ylsulfamide (7). The title compound was prepared from N-benzyl-2-oxooxazolidine-3-sulfonamide (3.51 g, 13.7 mmol) and N-benzylbut-3-en-2-ylamine (2.43 g,
15.1 mmol) according to general procedure A. This procedure afforded 2.90 g (64%) of the title compound as a white solid: mp = 46–48 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.41 (d, J = 7.2 Hz, 2 H), 7.37–7.25 (m, 6 H), 7.18 (dd, J = 1.7, 7.8 Hz, 2 H), 6.02 (ddd, J = 5.4, 10.6, 17.3 Hz, 1 H), 5.30–5.20 (m, 2 H), 4.55 (ddt, J = 1.7, 5.5, 7.1 Hz, 1 H), 4.38 (d, J = 15.5 Hz, 1 H), 4.26 (d, J = 15.6 Hz, 1 H), 4.07–3.96 (m, 3 H), 1.34 (d, J = 6.9 Hz, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 138.3, 136.6, 128.7, 128.5, 128.2, 127.9, 127.8, 127.5, 117.1, 56.3, 48.1, 47.2, 17.7; IR (film) 3273, 1316, 1150 cm⁻¹. MS (ESI) 331.1479 (331.1475 calcd for C₁₈H₂₂N₂O₂S, M + H⁺).

1,3-Bis-benzyl-1-methallylsulfamide (9). The title compound was prepared from N-benzyl-2-oxooxazolidine-3-sulfonamide (1.28 g, 5 mmol) and N-benzylmethallylamine (0.89 g, 5.5 mmol) according to general procedure A. This procedure afforded 1.29 g (78%) of the title compound as a white solid: mp = 59–60 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.41–7.28 (m, 8 H), 7.26–7.23 (m, 2 H), 5.00 (s, 1 H), 4.95 (s, 1 H), 4.39 (s, 2 H), 4.21 (s, 1 H), 4.13 (s, 2 H), 3.77 (s, 2 H), 1.76 (s, 3 H); ¹³C NMR (126 MHz, CDCl₃) δ 140.2, 136.7, 136.3, 129.0, 128.7, 128.6, 127.9, 127.9, 114.8, 53.5, 50.7, 47.3, 20.1; IR (film) 3289, 1317, 1132 cm⁻¹. MS (ESI) 331.1477 (331.1475 calcd for C₁₈H₂₂N₂O₂S, M + H⁺).

1,3-Bis-benzyl-1-cinnamylsulfamide (11). The title compound was prepared from N-benzyl-2-oxooxazolidine-3-sulfonamide (1.03 g, 4.0 mmol) and N-benzylcinnamylamine (0.98 g, 4.4 mmol) according to general procedure A. This procedure afforded 1.01 g (64%) of the title compound as a white solid: mp = 87–90 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.42–7.24 (m, 15 H), 6.45 (d, J = 15.9 Hz, 1 H), 6.15 (dt, J = 6.9, 15.8 Hz, 1 H), 4.44 (s, 2 H), 4.36 (t, J = 6.2 Hz, 1 H), 4.23 (d, J = 6.0 Hz, 2 H), 3.93 (d, J = 7.0 Hz, 2 H); ¹³C NMR (126 MHz, CDCl₃) δ 136.7, 136.3,
(Z)-1-(3-d-Allyl)-1,3-bis-benzylsulfamide (14). A flame dried round bottom flask equipped with a stirbar was cooled to rt under a stream of N₂ and charged with N-allylbenzylamine (10.0 mmol, 1.47 g) and Et₂O (20 mL). The resulting solution was cooled to −42 °C using a CO₂/CH₃CN bath and stirred for 5 min. A solution of n-BuLi in hexanes (7.5 mL, 1.6 M, 12 mmol) was added slowly and the resulting mixture was stirred at −42 °C for 20 min. A solution of t-BuLi in hexanes (13.75 mL, 1.6 M, 22 mmol) was added slowly and the resulting solution was stirred at −42 °C for 30 min. The CO₂/CH₃CN bath was replaced with a brine/ice bath and the reaction mixture was allowed to slowly warm to room temperature as the ice melted. The bath was removed and the mixture was stirred at rt for 1 h. The reaction mixture was then cooled to −78 °C and D₂O (3.6 mL, 200 mmol) from freshly cracked ampoules was slowly added. The resulting mixture was warmed to rt and stirred overnight. The reaction mixture was cooled to 0 °C, quenched with H₂O (15 mL) and transferred to a separatory funnel. The mixture was extracted with Et₂O (2 x 10 mL), the organic layers were combined and extracted with 1M HCl (3 x 10mL), and the organic layers were then discarded. The aqueous layers were combined, taken to pH 12 with 1M NaOH (40 mL), and extracted with CH₂Cl₂ (3 x 10mL). The combined organic layers were dried with anhydrous Na₂SO₄, filtered, and concentrated in vacuo to yield crude (Z)-N-(3-d-allyl)benzylamine.

A flame dried flask was then charged with 1-allyl-1,3-bis-benzylsulfamide (2.56 g, 10 mmol), 4-dimethylaminopyridine (244 mg, 2 mmol), and a stirbar, then was evacuated and backfilled with N₂. Acetonitrile (50mL) was added, followed by Et₃N (4.2 mL, 30 mmol), and then the reaction vessel was placed in an oil bath at 80 °C and stirred for 30 minutes. The crude amine was added and the resulting mixture was heated to reflux overnight (approximately 16 hours). The mixture was cooled to rt, solvent was removed via rotary evaporation, and the residue was partitioned between CH₂Cl₂ and 1 M HCl. The aqueous layer was extracted with CH₂Cl₂, the combined organics were washed with brine, dried with Na₂SO₄, filtered, and concentrated in
vacuo. The resulting crude product was purified by flash chromatography on silica gel to yield 1.20 g (38%) of the title compound as an off-white solid, mp = 52–54 °C. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.36–7.25 (m, 10 H), 5.80 (tdd, $J = 2.4$, 4.7, 9.0 Hz, 1 H), 5.21 (dt, $J = 1.1$, 10.2 Hz, 1 H), 4.38 (s, 2 H), 4.27 (t, $J = 6.1$ Hz, 1 H), 4.16 (d, $J = 6.0$ Hz, 2 H), 3.75 (d, $J = 6.7$ Hz, 2 H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 136.7, 136.2, 132.6, 128.8, 128.6, 128.6, 128.0, 127.9, 127.8, 119.3 (t, $J = 23.8$ Hz), 50.6, 49.8, 47.3; IR (film) 3257, 1299, 1142 cm$^{-1}$. MS (ESI) 318.1387 (318.1381 calcd for C$_{17}$H$_{19}$DN$_2$O$_2$S, M + H$^+$).

(E)-Dec-1-en-1-yl trifluoromethanesulfonate. The title compound was prepared from decanal (1.88 mL, 10 mmol), 2,6-di-tert-butylpyridine (2.65 mL, 12 mmol), and triflic anhydride (1.85 mL, 11 mmol) in DCE according to a procedure analogous to that described by Stang.$^{12}$ This procedure afforded 1.21 g (42%) of the title compound as a colorless oil. This compound was obtained as an 5:1 mixture of E:Z isomers as judged by $^1$H NMR analysis. Data are for the mixture. $^1$H NMR (500 MHz, CDCl$_3$) δ 6.56-6.46 (m, 1.2 H), 5.77 (dt, $J = 7.7$, 11.7 Hz, 0.2 H), 5.25 (td, $J = 5.6$, 7.6 Hz, 1.0 H), 2.19 (qd, $J = 1.6$, 7.5 Hz, 2.0 H), 2.04 (qd, $J = 1.5$, 7.5 Hz, 0.4 H), 1.40 (p, $J = 7.1$ Hz, 2.4 H), 1.36–1.20 (m, 12.0 H), 0.88 (t, $J = 6.8$ Hz, 3.6 H); $^{13}$C NMR (126 MHz, CDCl$_3$) δ 135.8, 135.1, 122.9, 120.8, 118.6 (q, $J = 320.7$ Hz), 31.8, 29.2, 29.1, 29.0, 28.8, 28.6, 28.5, 26.5, 24.1, 22.6, 14.0; IR (film) 2926, 1422, 1204, 1142 cm$^{-1}$. MS (ESI) 287.0928 (287.0934 calcd for C$_{11}$H$_{19}$F$_3$O$_3$S, M + H$^+$).
Assignment of Stereochemistry

Sulfamide 13

The stereochemistry of 13 was assigned on the basis of 1D NOESY experiments. The key nOe signals are shown below.

Sulfamides 15, 19

The stereochemistry of deuterated products 15 and 19 were assigned on the basis of 1D NOESY experiments carried out with the all-proteo analog of these compounds. The key nOe signals are shown below. The stereochemistry of the deuterated products was then assigned by examining which signal in each product was absent from the $^1$H NMR spectrum.

To provide further support for the assignments of 15 and 19, these compounds were converted to the corresponding ureas via reduction with LiAlH$_4$ and carbonylation with CDI. The proton NMR spectra of S2 (the urea derived from 15) was similar to that of 22, whereas the proton NMR spectr of S3 (the urea derived from 19) was similar to that of 21, with respect to the relative chemical shifts of the aliphatic protons and the coupling constants. Data for S2 and S3 are provided below.
(±)-(1'S,3S)-2,3,5-Tribenzyl-1'-deuterioimidazolidin-2-one (S3). 75 mg (0.19 mmol) of 15 was cleaved with LiAlH₄ using a procedure similar to that of Chemler. The crude product was dissolved in 1 mL THF and CDI (0.29 mmol, 47.0 mg) in 1 mL THF was added and brought to reflux for 24 h. Solvent was then removed and the product was purified by flash chromatography on silica gel to afford 34 mg (50%) of the title compound as a clear colorless oil. ¹H NMR (700 MHz, CDCl₃) δ 7.40–7.14 (m, 13 H), 6.95 (d, J = 7.0 Hz, 2 H), 4.94 (d, J = 15.1 Hz, 1 H), 4.40 (d, J = 14.8 Hz, 1 H), 4.36 (d, J = 15.0 Hz, 1 H), 4.14 (d, J = 15.1 Hz, 1 H), 3.61–3.54 (m, 1 H), 3.05–2.99 (m, 2 H), 2.86 (dd, J = 6.9, 9.0 Hz, 1 H); ¹³C NMR (176 MHz, CDCl₃) δ 160.7, 137.4, 137.2, 136.6, 129.0, 128.6, 128.5, 128.2, 127.9, 127.4, 127.3, 126.7, 53.5, 48.1, 47.5, 46.0, 38.2 (t, J = 20.0 Hz); IR (film) 1685 cm⁻¹. MS (ESI) 358.2026 (358.2024 calcd for C₂₄H₂₃DN₂O, M + H⁺).

(±)-(1'R,3S)-2,3,5-Tribenzyl-1'-deuterioimidazolidin-2-one (S4). 45 mg (0.11 mmol) of 19 was cleaved LiAlH₄ using a procedure similar to that of Chemler. The crude product was dissolved in 1 mL THF and CDI (0.17 mmol, 27.6 mg) in 1 mL THF was added and brought to reflux for 24 h. Solvent was then removed and the product was purified by flash chromatography on silica gel to afford 28 mg (71%) of the title compound as a clear colorless oil. ¹H NMR (700 MHz, CDCl₃) δ 7.38–7.13 (m, 13 H), 6.95 (d, J = 7.1 Hz, 2 H), 4.93 (d, J = 15.1 Hz, 1 H), 4.39 (d, J = 15.0 Hz, 1 H), 4.36 (d, J = 15.0 Hz, 1 H), 4.13 (d, J = 15.3 Hz, 1 H), 3.60–3.53 (m, 1 H), 3.05–3.00 (m, 1 H), 2.86 (dd, J = 6.9, 8.9 Hz, 1 H), 2.56–2.46 (m, 1 H); ¹³C NMR (176 MHz, CDCl₃) δ 160.7, 137.3, 137.2, 136.6, 129.0, 128.6, 128.5, 128.2, 127.9, 127.4, 127.3, 126.7, 53.5, 48.1, 47.5, 46.0, 38.3 (t, J = 20.0 Hz); IR (film) 1685 cm⁻¹. MS (ESI) 358.2026 (358.2024 calcd for C₂₄H₂₃DN₂O, M + H⁺).
Ureas 21 and 22

The stereochemical assignment of urea 21 has been previously reported. The stereochemistry of deuterated urea 22 was assigned on the basis of 1D NOESY experiments. The key nOe signals are shown below. The stereochemistry of the deuterated products was then assigned by examining which signal in each product was absent from the $^1$H NMR spectrum.

![Urea Structures](image)

Sulfamide 8

The stereochemistry of sulfamide 8 was assigned on the basis of 1D NOESY experiments. The key nOe signals are shown below.

![Sulfamide Structure](image)

Ar = $p$-CNC$_6$H$_4$

References


S1c